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Press Room, Oct. 17–21: (312) 791-6619

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NEW STUDIES OFFER GREATER INSIGHT INTO HOW THE BRAIN PROCESSES FACIAL INFORMATION AND SOCIAL CUES

CHICAGO — Humans are very social creatures and the ability to identify and "read" faces is central to all successful social interactions. Research released today on how the brain recognizes and processes facial data contributes to our understanding of social interaction and how it goes awry in neurodevelopmental disorders such as autism, as well as Williams, Rett's, Fragile X, and Timothy syndromes. This research also adds to a relatively new and growing area of inquiry — social neuroscience, which investigates the brain mechanisms underlying social processes and behaviors.

The findings were presented at Neuroscience 2009, the Society for Neuroscience's annual meeting and the world's largest source of emerging news about brain science and health.

The new findings show that:

- People with agenesis of the corpus callosum (AgCC), a rare neurological disorder, look at faces in a way that impairs their ability to determine people's emotions. This finding offers one explanation for why individuals with AgCC have such difficulty picking up on the social cues of others and suggests a possible factor in the development of autism, a more common neurological disorder with similar symptoms (Lynn K. Paul, PhD, abstract 209.8, see attached summary).
- The response pattern of neurons in the visual areas of the brain can predict the ethnicity of the person being looked at, laying the foundation for understanding differences in the way our brains represent faces from people of our own race versus faces from other races (Vaidehi Natu, abstract 168.13, see attached summary).
- Recognizing gender is an important social cue and research into female macaque monkeys shows that humans are not alone in distinguishing gender from facial images alone (Kari Hoffman, PhD, abstract 168.2, see attached summary).

Other recent research findings being discussed at the meeting show that:

- Researchers have identified mutations in synaptic proteins in some people with autism. These findings suggest that autism affects the wiring of the developing brain (Thomas C. Südhof, MD, see attached speaker's summary).
- Williams syndrome, a hyper-social disorder often called the opposite of autism, is caused by a genetic mutation. Research into the disorder may provide new insight on how genes are translated in the brain to produce cognitive and behavioral features (Karen F. Berman, MD, see attached speaker's summary).

"The brain makes it possible to successfully communicate and interact with our surroundings," said press conference moderator David Amaral, research director of the M.I.N.D. Institute at the University of California, Davis, PhD, an expert on neural development disorders. "Social neuroscience highlights the fundamental role of communication on a cellular and molecular level, and further research will inform us about the mind, behavior, and neurodevelopmental disorders."

This research was supported by national funding agencies, such as the National Institutes of Health, as well as private and philanthropic organizations.

– more –

Related Presentations:

Special Lecture: **From Synapses to Autism: Neurexins, Neuroligins, and More**
Sunday, Oct. 18, 1–2:10 p.m., Hall B1

Special Lecture: **Understanding Neurogenetic Mechanisms in Neuropsychiatric Conditions: Lessons from Williams Syndrome**
Tuesday, Oct. 20, 1–2:10 p.m., Hall B1

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Abstract 209.8 Summary

Lead author: Lynn K. Paul, PhD (626) 395-4077
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New Research Shows Rare Neurological Condition Impairs Ability to Read Facial Emotions

Findings suggest people with developmental brain malformations and those with autism may share face-processing impairments

People with agenesis of the corpus callosum (AgCC), a rare neurological condition, look at faces in a way that impairs their ability to determine people's emotions, according to a new study. This may explain why these individuals have difficulty reading social cues and also suggests a developmental factor in autism, which has similar symptoms. The study was presented at Neuroscience 2009, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health.

"We found that these individuals do not examine other people's eyes normally when scanning faces to identify emotion," said Lynn K. Paul, PhD, at the California Institute of Technology and the study's lead author. "This may contribute to their difficulty naming emotions and performing in social situations."

AgCC, which affects about 1 in 2,000 people, is diagnosed when the corpus callosum, the main route connecting the two brain hemispheres, is totally or partially missing. Collaboration between the two highly specialized sides of the brain then breaks down, resulting in difficulties with complex social processes, such as identifying what others are feeling or intending.

Nine adults with primary AgCC and nine without participated in the study. They were shown photos of faces and asked to perform several tasks. Although the AgCC participants were accurate in identifying gender, they were not as good at naming emotions, especially fear and anger. Eye-tracking measurements showed they spent less time looking at eyes and more looking at the nose and mouth regions. In addition, when shown a new face, the AgCC group took longer to look at eyes.

Previous research has shown that people with autism are also more likely to look at the mouth than the eyes when scanning faces. "This similarity suggests that autism may result from impaired collaboration between brain areas, as some scientists have proposed," said Paul.

Scientific Presentation: Sunday, Oct. 18, 2:45–3 p.m., Room S103

209.8, Identifying facial emotions in agenesis of the corpus callosum
L. K. PAUL[1], M. BRIDGMAN[1], W. S. BROWN[2], M. L. SPEZIO[3], R. ADOLPHS[1]; [1]Caltech, Pasadena, CA; [2]Travis Res. Institute, Fuller Theological Seminary, Pasadena, CA; [3]Scripps Col., Pomona, CA

TECHNICAL ABSTRACT: Agenesis of the corpus callosum (AgCC) is a congenital condition in which the ~190 million fibers that normally connect the cerebral hemispheres fails to develop. Primary AgCC is characterized by minimal additional neuropathology and intact intelligence. However, individuals with Primary AgCC exhibit deficits in non-literal language comprehension, humor, theory of mind, and social reasoning (Paul et al., 2007). The symptom profile of Primary AgCC is similar to autism, particularly the impairments in social interaction and communication (Badaruddin et al., 2007). In autism research, psychosocial deficits have been related to atypical facial scanning and impaired emotion recognition (Pelphrey et al., 2002), skills which we have now examined in Primary AgCC. Nine adults with Primary AgCC and 9 controls completed 4 tasks with Ekman emotional faces: emotion recognition of upright faces and inverted faces, gender naming, and passive viewing. Participants were assessed for accuracy on the three recognition tasks. Eye-movement data were gathered with Eyelink II eye-tracking system and analyzed on all four tasks according to examiner designated facial regions of interest for frequency of fixations and duration of fixations. Overall the AgCC group was less accurate than controls in naming all emotions, especially fear and anger, for both upright and inverted faces. The AgCC group exhibited an inversion effect for emotion recognition, and showed a greater decline in performance than controls on happy, neutral and fearful inversions. For upright faces, the AgCC group had smaller fractional dwell times and fewer fixations in the eye regions, and larger fractional dwell times and more fixations in the nose and mouth regions, compared to controls. Distribution of fixations across the trial indicates that control subjects generally fixated the eyes earlier in the trial than did AgCC subjects. AgCC subjects did not differ from controls in accuracy of gender identification, nor did they have significant differences in eye-tracking patterns. Thus, as seen in autism, it appears that individuals with AgCC do not examine others' eyes normally when scanning faces to identify emotion, which may contribute to their impaired emotion identification and psychosocial impairments in general.

Abstract 168.13 Summary

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Research Suggests Faces of Different Races Activate Different Brain Patterns

Finding is a prerequisite for understanding difficulty recognizing other-race faces

Predicting whether a person is looking at an Asian or Caucasian face can be determined solely from the response patterns that neurons make in the visual areas of the viewer's brain, a new study has found. Understanding how our brains respond to faces of different races may help to explain why people — including crime eyewitnesses — make more mistakes recognizing faces of other races than their own.

"When we fail to see what makes a person's face unique, we are at risk for treating them as a member of a 'group' rather than as an unique individual," said lead author Vaidehi Natu of the University of Texas at Dallas. "At best, this problem creates embarrassing social situations. At worst, its consequences can be devastating, such as in the courtroom."

Natu and her colleagues used functional magnetic resonance imaging (fMRI) to measure neural activity for five Asians and five Caucasians while they were looking at Asian and Caucasian faces. For each participant, the researchers developed a mathematical algorithm to "learn" the features of the person's brain activity patterns that could predict whether the person was viewing an Asian or Caucasian face. They then tested the algorithm by having the participants look at a new series of faces.

"We found that the neural patterns evoked by Asian and Caucasian faces were different enough to be separable at levels above chance in the brains of both groups," Natu said. "This finding opens the door for understanding how the embarrassing failures we sometimes experience in perceiving the uniqueness of other-race faces arise from the underlying neural representations that have been shaped by our experiences."

Research was supported by the Advanced Imaging Research Center at the University of Texas Southwestern Medical Center in Dallas, Texas.

Scientific Presentation: Sunday, Oct. 18, 8–9 a.m., South Hall A

168.13 Dissociable neural responses for Caucasian versus Asian faces using a pattern-classification approach
V. NATU, C. WOLFE, J. JAIN, A. J. O'TOOLE; Univ. Texas Dallas, Richardson, TX

TECHNICAL ABSTRACT: Neuroimaging studies that have examined the neural underpinnings of the other-race effect for faces have concentrated primary, but not exclusively, on the question of whether faces of different races activate the amygdala differentially (Cunningham et al., 2004; Hart et al., 2000; Lieberman et al., 2005). In addition to the social and emotive associations linked to race, there are also large-scale visual differences that support the initial categorization of race (Ng et al., 2007). Previous approaches to understanding the coding of face race in cortex have used either adaptation-based methods or methods that compare neural response strength for faces of different races in targeted brain areas. A more direct approach is to apply a pattern-based classifier to the task of discriminating the neural representations for faces by race. We examined the brain responses elicited in the visual areas of the ventral temporal (VT) cortex of Caucasian participants (n = 4) while they viewed Caucasian and Asian faces. The data were collected in an fMRI experiment in which participants saw alternating identity-constant blocks of Caucasian and Asian faces, presented with multiple frontal images of each identity. For each participant, a classifier was used to discriminate brain response patterns for Caucasian versus Asian faces. Voxels for the pattern-classifier were chosen based on significant variation across faces, objects, and scrambled images assessed in an independent localizer scan session. This method of voxel-selection provides a broad area of the VT cortex, including the fusiform gyrus, lateral occipital areas, and the superior temporal area. The data were subdivided into odd-even counterbalance runs for training and test and were analyzed with principal components analysis (PCA). Next, the scans were projected onto their PCs for input to the classifier. Dimensions useful for training set classification were combined and used for classifying the test sets. The neural activation maps elicited for Caucasian and Asian faces were discriminable at levels above chance for all participants. Moreover, in an analysis of the time-course of neural activation within race-constant blocks, same-race Caucasian faces elicited significantly more activation in the first TR of the block (Golby et al., 2001; Kim et al., 2006), but this pattern reversed subsequently with significantly greater activation for Asian faces across 12 of the remaining 14 TRs. Combined, these results suggest the importance of both spatial and temporal neural activation in understanding the neural codes involved in representing the visual characteristics of faces.

Abstract 168.2 Summary

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Female Interest in the Faces and Hindquarters of Both Sexes of Macaques

Study finds macaques share human ability to distinguish gender from faces

Are humans uniquely able to distinguish gender solely from looking at faces? Not according to new research being presented at Neuroscience 2009, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health, which found a similar ability in female macaque monkeys. Like human society, gender discrimination is critical in macaque society, but little has been known about how or whether macaques process the sex of others in their species.

Neuroscientist Kari Hoffman, PhD, and graduate student Kira Bucca, both of York University in Toronto, had a female rhesus macaque choose how long to gaze at an image of an unfamiliar macaque. The images were grouped into four categories: female and male faces, and female and male hindquarters that revealed external genitalia. "Our female macaque spent more time viewing male faces," Hoffman said. "She also spent more time viewing female hindquarters than female faces."

Surprisingly, this pattern resembles that of male monkeys in an earlier study from another research team. Although that study didn't directly compare gender differences in the responses to viewing images, it found that male macaques would "pay" (forego a reward) to view images of both male faces and female hindquarters.

In the current study, the female macaque was tested around the time of ovulation. Previous research suggests that female monkeys, like humans, show an increased preference for male faces while ovulating. But another possible explanation, said Hoffman, is that the male faces were perceived as threatening and thus warranted more attention than the female faces.

"More research on both sexes will be needed before speculating about whether all macaques show the preferences we found — and to what extent these preferences match those of humans," Hoffman said.

Scientific Presentation: Sunday, Oct. 18, 9–10 a.m., South Hall A

168.2 Looking preferences for the faces and hindquarters of both sexes in female macaques
K. A. BUCCA, H. A. CLAYTON, **K. L. HOFFMAN**; York Univ., Toronto, ON, Canada

TECHNICAL ABSTRACT: Neuronal and behavioral responses to faces and body parts have been researched extensively across several species. In humans, gender has been one important feature used to categories faces and bodies. In contrast, we know relatively little about how or whether rhesus macaques process the sex of conspecifics. In male macaques, familiar male faces and familiar female hindquarters were shown to be rewarding, though reward value has not been addressed across sex. Moreover, female macaques show an increase in preference for male faces during estrogen peaks [1], though their sex-preference for hindquarters is unknown. Here, using a balanced design, we tested the viewing preferences of one adult female macaque towards unfamiliar faces and hindquarters of both male and female conspecifics (N=8 exemplars per category). A trial consisted of a target image - the face or hindquarter of a given sex - that was alternated with a gray screen, changing each time the monkey looked away from the monitor, for a cumulative on-screen looking time of 8 seconds. We obtained a total of 60 trials per category over 8 daily sessions. We defined the preference ratio as the proportion of the cumulative looking time that was spent viewing the target image, and compared preference ratios for each category using a 2x2 ANOVA across sex (male, female) and body part (face, hindquarters) categories. There were no main effects of sex or body part, but we observed an interaction effect whereby male faces were preferred to female faces. There was also a preference for female hindquarters relative to female faces. Considered in isolation, the preference for male over female faces could be related to sexual receptivity, consistent with previous findings[1]; however, this account fails to explain why interest in hindquarters showed no sex bias, nor why female hindquarters were preferred to female faces. The interest in male faces may not be due to attraction in the hedonic or sexual sense, since male hindquarters, which displayed male genitalia, were not similarly attractive. Instead, the male face may have been perceived as threatening and therefore warranted more attention. Scan path analysis might reveal whether the face per se was being fixated differently across condition, or even differently across the viewing monkey's menstrual cycle. Although more females need to be tested, the observed bias towards male faces demonstrates that female macaques can discriminate the sex of conspecific faces.

[1] Lacreuse A, Martin-Malivel J, Lange HS, Herndon JG. Animal Cognition 2007 APR;10(2):105-15.

Speaker's Summary

Speaker: Thomas C. Südhof, MD (650) 721-1421
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Special Lecture: **From Synapses to Autism: Neurexins, Neuroligins, and More**
Sunday, Oct. 18, 1–2:10 p.m., Hall B1

Autism spectrum disorders affect 1 in 160 people; males are affected four times as frequently as females. Patients with these disorders suffer from impaired social interactions, verbal communication difficulties, repetitive stereotyped behaviors (such as also observed in obsessive-compulsive disorders), and restricted interests. A huge range of symptoms are observed, with vast differences in severity. Some affected individuals are functioning well in many tasks and exhibit primarily social interaction impairments (as found in Asperger's syndrome, or in a more extreme form in the 'savant' syndrome), whereas other individuals are basically incapacitated. Autism spectrum disorders are not apparent at birth, but manifest soon afterwards, and are usually diagnosed within the first three postnatal years. They are highly heritable (>75%), and also accompany other more serious developmental genetic disorders such as Rett's syndrome or fragile X syndrome. Because of their heritability and the recent advances in human genetics, many genes (>100) have been linked to autism spectrum disorders.

My presentation will focus on one set of genes that we discovered long before these genes were linked to autism spectrum disorders, but are now among the best characterized genes thought to be involved in their development. These are genes that encode neurexins and neuroligins, and that are involved in the development and maintenance of synapses. Synapses are the junctions between brain cells that allow these cells to communicate with each other. Brain cells form extensive parallel circuits that consist of networks of synapses, and that mediate human perception, thought, and behavior. Moreover, synapses are essential for learning and memory, and for all cognitive abilities. The formation, properties, and plasticity of synapses depend on proteins called synaptic cell-adhesion molecules that connect the brain cells at a synapse to each other. Neurexins and neuroligins are synaptic cell-adhesion molecules, in fact are arguably the best characterized synaptic cell-adhesion molecules at present. Their genes are not infrequently mutated in individuals with autism spectrum disorders, which will be part of the subject of my talk, prompting us to study their role in brain in detail.

At synapses, neurexins and neuroligins form trans-synaptic complexes that are essential for specifying the diverse properties of the synapses in a neural circuit. Neurexins are primarily presynaptic, and neuroligins postsynaptic; both are required for survival of an animal or person. Extracellularly, the trans-synaptic neurexin/neuroligin complex forms the nucleus for multifarious interactions with other synaptic proteins, explaining the diverse functions of neurexins and neuroligins that are only partly dependent on their interactions. Intracellularly, the neurexin/neuroligin complex binds other proteins that link neurexins and neuroligins to signaling molecules that mediate the ability of a synapse to transfer a signal from one brain cell to the next brain cell. The central role of the neurexin/neuroligin complex in neural circuits is apparent from the synaptic impairments observed in mutant mice in which components of this complex are absent, and highlighted by accumulating evidence linking the neurexin/neuroligin complex to autism spectrum disorders. Specifically, more than 10 families were described with familial forms of autism carrying mutations in the neuroligin-4 gene, and one family with a point mutation in the neuroligin-3 gene. Moreover, 0.5% of individuals with autism spectrum disorder lack one copy of the neurexin-1α gene. Furthermore, mutant mice in which neuroligin is abnormal exhibit many symptoms that at least partly resemble those observed in autism spectrum disorder phenotypes, consistent with the notion that neuroligins and neurexins perform functions that are impaired in autism spectrum disorder. Translating these findings into any practical diagnostic or therapeutic approaches will require much additional work, but we feel that understanding the relations between specific genes that are abnormal in at least some individuals with autism spectrum disorders and brain function will provide progress in understanding the pathogenesis of these important disorders.

Speaker's Summary

Speaker: Karen F. Berman, MD (301) 496-7604
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Special Lecture: **Understanding Neurogenetic Mechanisms in Neuropsychiatric Conditions: Lessons from Williams Syndrome**
Tuesday, Oct. 20, 1–2:10 p.m., Hall B1

Recent advances in identifying genetic contributions to complex, common neuropsychiatric disorders have made clear that the stage is set for unprecedented progress in elucidating fundamental mechanisms of brain function and dysfunction. The next challenge is to unravel the functional implications of genetic variation within the context of clinical neurobiology. Understanding such neurogenetic mechanisms holds considerable promise for identifying new pathways to prevention and treatment.

Williams syndrome, a rare neurogenetic disorder caused by hemizygous microdeletion of approximately 1.6 megabases on chromosomal band 7q11.23, typically by spontaneous mutation, offers a unique window onto gene-brain-behavior mechanisms. With its unique profile of striking behavioral features, such as remarkable hypersociability combined with differential impact on cognitive functions — some only mildly affected while others, particularly visuospatial construction, are severely impaired — Williams syndrome is an intriguing experiment of nature that offers fundamental insights about neurogenetic mechanisms of cognition and social behavior, as well as about brain plasticity during development. Because the genes involved in Williams syndrome are known, the study of neural mechanisms in Williams syndrome affords a privileged setting for investigating genetic influences on complex brain functions.

Neuroimaging, with its increasingly rich and incisive armamentarium of tools for deriving molecular, structural, and neurofunctional information, can be used to investigate how genetic variability is translated in the brain to produce cognitive and behavioral features. With multimodal imaging, we have identified a number of fundamental aspects of the brain phenotype in Williams syndrome: 1) underlying the syndrome's cognitive hallmark, visuospatial construction impairment, is a neurostructural anomaly (decreased gray matter volume) and adjacent abnormal neural functional in the parietal sulcus region of the dorsal visual processing stream; 2) also contributing to the visuospatial problems are hippocampal abnormalities in regional cerebral blood flow, neurofunctional activation, and N-acetyl aspartate concentration (measured *in vivo* with MR spectroscopy), as well as subtle structural changes; 3) underlying the syndrome's hallmark social cognition features are structural and functional abnormalities in the orbitofrontal cortex, an important affect and social regulatory region that participates in a fronto-amygdalar regulatory network found to be dysfunctional in Williams syndrome; and 4) as an underpinning for several of these gray matter structural and functional abnormalities, white matter axonal tracts (measured *in vivo* with MR diffusion tensor imaging) have been found to be abnormal. Identification of these brain phenotypes provides an avenue for linking dosage of specific genes in 7q11.23, such as *LIMK1* and *CLIP2*, which are involved in neuronal maturation and migration, to the neural, and thus to the behavioral features of the syndrome. This model approach extends and complements efforts to understand genetic mechanisms of behavior, and its pathologies, in the general population, where contributions of individual genes may be small and phenotypes may be subtle and complex.